Amendments to the Specification

Page 17, lines 19-26, please rewrite as follows:

HPLC analyses were performed on a Merck-Hitachi L-7000 system equipped with a EG&G Berthold LB 508 radiometric detector, using Waters XTerra RP8 columns (5 ~~m~~ µm particle size, 1 x 100 mm) and a flow rate of 1 ml/min. Chromatograms were recorded at 250 and 360 nm. Solvent a were predominantly aqueous buffers. Sodium acetate buffer a was prepared by mixing 2.9 ml acetic acid and 4.55 ml sodium hydroxide 2 M in 900 ml water and 100 ml methanol. Tris buffer a was prepared by dissolving tris(hydroxymethyl)aminomethane (605 mg) in water, adding HCl 2 M to reach a pH of 8.2, adjusting the volume to in 1000 ml, and adding acetonitrile (10 ml). Solvent b was always methanol.

Page 17, lines 28-31, please rewrite as follows:

Preparative HPLC separations were performed on a Varian Prostar system equipped with two Prostar 215 pumps and a Prostar 320 UV/Vis detector, using Waters XTerra Prep RP8, columns (5 ~~m~~ µm particle size, 3 x 100 mm and 30 x 100 mm). Flow rates were 4 ml/min for the 3 x 100 mm column and 30 ml/min for the 30 x 100 mm column.

Page 18, line 33 to page 19, line 8, please rewrite as follows:

Example 1: Cyanocobalamin monocarboxylic acids (*b*, *d* and *e*)

Vitamin B12 (1.88 g, 1.39 mmol) is hydrolyzed in HCl 0.1 M (190 ml) as described by Pathare et al. (Bioconjugate Chem. 1996, 217). The purification is modified in the following way: The Dowex column allows, after desalting by phenol extractions, the isolation of three fractions, one containing exclusively *d*-acid, a second one containing exclusively *b*-acid and *d*-acid, a third one exclusively *b*-acid and *e*-acid. The mixture of *b*-acid and *d*-acid is separated by preparative HPLC (column: Waters XTerra Prep RP8, 5 ~~m~~ µm, 30 x 100 mm; gradient a/b 0.5% min^{-1} starting from 100% acetate buffer a). The mixture of *b*-acid and *e*-acid is separated on the same system but using the Tris buffer as solvent a. Cyanocobalamin-*b*-acid is isolated in a yield of 280.6 mg (14.9%), cyanocobalamin-*d*-acid in a yield of 131.5 mg (7.0%), and cyanocobalamin-*e*-acid in a yield of 94.26 mg (5.0%).

Page 19, lines 10-23, please rewrite as follows:

Example 2: Cyanocobalamin-*b*-(2-aminoethyl)amide [cyanocobalamin-*b*-ethylamine]

Cyanocobalamin-*b*-(2-aminoethyl)amide was prepared as described by Pathare et al. (Bioconjugate Chem. 1996, 217) for the synthesis of the dodecane analog. Ethylene diamine (132 mg; 0.147 ml; 2.2 mmol) was dissolved in a DMF/H_2O mixture (10 ml; 1/1 v/v). The pH was adjusted to 5 by addition of 1 M HCl. To the solution were added cyanocobalamin-*b*-acid (60.0 mg, 44.4 ~~mol~~ µmol) and KCN (57 mg; 0.87 mmol), followed by adjustment of the pH to 5.5. Next, EDC (84.2 mg; 0.43 mmol) and HOSu (50.6 mg; 0.44 mmol) were added. The mixture was stirred at RT for 3 days, and extra portions of EDC and HOSu were added at 24 h intervals. For the work-up, the mixture was evaporated to dryness *in vacuo*, followed by preparative HPLC purification (acetate system, gradient: 0.5% min^{-1} starting from 100% buffer a) to afford 34 mg (55%) of cyanocobalamin-*b*-(2-aminoethyl)amide.

MS (MeOH; ESI-pos.): m/z = 1398.8 $[M+H]^+$, 1420.1 $[M+Na]^+$, 699.4 $[M+H]^{2+}$, 711.1 $[M+H+Na]^{2+}$.

Page 19, lines 29-36, please rewrite as follows:

Example 4: Cyanocobalamin-*b*-ethyl-PAPAcet

Cyanocobalamin-*b*-ethylamine (Example 2; 24 mg; 17.2 µmol) was dissolved in a DMF/DMSO mixture (5 ml; 4/1 v/v). To this mixture was added 3-[*N*-2-cyanoethoxy-carbonylmethyl-*N*-pyridin-2-ylmethyl-amino]-propionic acid 4-nitrophenyl ester (14 mg, 34.1 ~~mol~~ µmol) and DIPEA (5 ~~l~~ µl, 29 ~~mol~~ µmol). After stirring at RT for 24 h, the mixture was evaporated to dryness *in vacuo*. Purification by preparative HPLC (acetate system, gradient: 0.5% min^{-1} starting from 100% buffer a) afforded 20 mg (70%) cyanocobalamin-*b*-ethyl-PAPAcet as a red solid.

Page 20, lines 3-14, please rewrite as follows:

Example 5: Cyanocobalamin-*b*-butyl-PAPAcet

Cyanocobalamin-*b*-butylamine (Example 3, 5.5 mg, 3.9 ~~mol~~ µmol) and 3-[*N*-2-cyanoethoxycarbonylmethyl-*N*-pyridin-2-ylmethyl-amino]propionic acid 4-nitrophenyl ester (2.5 mg, 6.1~~mol~~ µmol) were dissolved in a mixture of dry DMSO (0.5 ml) and DMF (0.5 ml). DIPEA (5 ~~l~~ µl, 29 ~~mol~~ µmol) was added to reach a pH between 8 and 9, and the mixture was stirred at room temperature. After 5 h, HPLC analysis confirmed complete product formation. The solvent was partially evaporated *in vacuo* to allow the

product to precipitate upon addition of ethyl ether. The suspension was centrifugated and decanted three times to give a fine powder. Purification by preparative HPLC (acetate system, gradient: 0.5% min^{-1} starting from 100% buffer a) gave the pure product in an yield of 2.7 mg (41%).

ESI-MS: m/z = 850.1 $[M+2]^{2+}$

UV/Vis: ~~nm~~ λ/nm (~~/mol~~ ε/mol $l^{-1}cm^{-1}$) = 279.1 (17300), 361.0 (31200), 519.9 (8700), 552.0 (9700).

Page 20, lines 16-28, please rewrite as follows:

Example 6: Cyanocobalamin-*b*-butyl-aminocarboxymethyl-His-OMe

A solution of cyanocobalamin-*b*-butylamine (49.6 mg, 34.8 ~~mol~~ µmol) in dry DMSO (2 ml) was added to methyl 1-carboxymethyl-*N*-Fmoc-histinate hydrochloride (35.5 ~~mol~~ µmol) and BOP (46.2 mg, 104.4 ~~mol~~ µmol). DIPEA (12 ~~l~~ µl, 70.0 ~~mol~~ µmol) was added, and the solution was stirred at RT for 16 h. HPLC analysis confirmed full conversion of the cobalamin starting material into the Fmoc protected intermediate. The intermediate was precipitated by adding diethyl ether, and the suspension was centrifugated and decanted trice to give a fine powder. The intermediate was dissolved in DMF (5 ml), and piperidine (225 ~~l~~ µl) was added. After stirring at RT for 1.5 h, the product was precipitated by adding diethyl ether, and the suspension was centrifugated and decanted three times to give a fine powder. Purification by preparative HPLC (acetate system, gradient: 1% min^{-1} starting from 100% buffer a) gave the pure product in a yield of 17.1 mg (32.1%).

UV/Vis: ~~nm~~ λ/nm (~~/mol~~ ε/mol $l^{-1}cm^{-1}$) = 279.1 (19200), 361.0 (24700), 521.0 (9600), 551.1 (10700).

Page 20, line 30 to page 21, line 6, please rewrite as follows:

Example 7: Cyanocobalamin-*c*-(4-aminobutyl)-amide [cyanocobalamin-*c*-butylamine]

Cyanocobalamin-*c*-acid was prepared as described by Brown et al. (Inorg. Chem. 1995, 3038). 1,4-Diaminobutane (0.059 ml; 0.59 mmol) was dissolved in a DMF/H_2O mixture (10 ml; 1/1 v/v). The pH was adjusted to 5.2 by addition of 1 M HCl. To the solution were added cyanocobalamin-*c*-acid (16.0 mg, 11.8 ~~mol~~ µmol), KCN (15.3 mg; 0.236 mmol), EDC (9.0 mg; 47.2 ~~mol~~ µmol) and HOSu (5.4 mg; 47.2 ~~mol~~ µmol). The mixture was stirred at RT for 4 days, and extra portions of EDC and HOSu were added. After another day, extra portions of EDC and HOSu were added again. After a total of 6 days, HPLC

analysis confirmed complete conversion of the cobalamin derivative. For the work-up, the mixture was evaporated to dryness *in vacuo*, followed by preparative HPLC purification (RP C18 column, HCl 1 mM as buffer a, gradient: from 20% methanol to 50% methanol in 30 minutes) to afford 9.8 mg (58%) of cyanocobalamin-*c*-butylamine.
MS (MeOH; ESI-pos.): m/z = 1427.7 $[M+2]^+$, 713.5 $[M+1]^{2+}$.

Page 21, lines 8-14, please rewrite as follows:

Example 8: Cyanocobalamin-*c*-butyl-PAPAcet

Cyanocobalamin-*c*-butylamine (7.0 mg, 4.9 ~~mol~~ µmol) and 3-[*N*-2-cyanoethoxycarbonylmethyl-*N*-pyridin-2-ylmethyl-amino]propionic acid 4-nitrophenyl ester (3.8 mg, 9.2 ~~mol~~ µmol) were reacted and purified as described in the synthesis of cyanocobalamin-*b*-butyl-PAPAcet (Example 5) to give the pure product in an yield of 3.8 mg (78%).
ESI-MS: m/z = 1701.0 $[M+1]^+$, 850.1 $[M+1]^{2+}$.
UV/Vis: ~~nm~~ λ/nm (~~/mol~~ ε/mol l^{-1} cm^{-1}) = 278.1 (14500), 362.1 (25400), 550.0 (7900).

Page 21, lines 16-26, please rewrite as follows:

Example 9: Cyanocobalamin-*b*-butyl-PAPA-$Re(CO)_3$

Cyanocobalamin-*b*-butylamine (Example 3, 24.6 mg, 17.2 ~~mol~~ µmol) and $Re(CO)_3$(3-[*N*-carboxymethyl-*N*-pyridin-2-ylmethyl-amino]propionic acid) (9.1 mg, 17.2 ~~mol~~ µmol) were dissolved in DMSO. BOP (22.9 mg, 51.7 ~~mol~~ µmol) and DIPEA (2.94 ~~l~~ µl, 17.2 ~~mol~~ µmol) were added, and the mixture was stirred at room temperature. DIPEA and BOP were added daily during 4 days. HPLC analysis confirmed formation of two products. They were precipitated upon addition of ethyl ether. The suspension was centrifugated and decanted three times to give a fine powder. Purification by preparative HPLC (acetate system, gradient: 0.5% min^{-1} starting from 100% buffer a) allowed the isolation of the main product peak in a yield of 2.3 mg (7.0%).
ESI-MS: m/z = 1917.5 $[M+2]^+$, 959.9 $[M+4]^{4+}$.

Page 21, line 28 to page 22, line 3, please rewrite as follows:

Example 10: Cyanocobalamin-*b*-ethyl-PAMA-OEt

Cyanocobalamin-*b*-acid (20.0 mg, 14.8 ~~mol~~ µmol) was dissolved in DMSO (0.8 ml). Subsequently were added DMF (2 ml) and NEt_3 (0.1 ml). In a different flask *ca.* 5 equivalents of (*N*-2-aminoethyl-*N*-pyridin-2-ylmethyl-amino)acetic acid ethyl ester (ethyl-

PAMA-OEt) hydrochloride (prepared via cleavage of the Boc-protected derivative by stirring in an abs. EtOH / 2 M HCl mixture (7.5 ml 4/1 v/v) overnight and subsequent removal of the volatiles *in vacuo*) was dissolved in a DMF/NEt_3 mixture (4.5 ml; 8/1 v/v). The two solutions were mixed, followed by addition of TBTU (32.1 mg, 0.1 mmol). After stirring at RT for 45 min, the solvent was removed *in vacuo*. The residue was purified by preparative HPLC (acetate system, gradient: 1.0% min^{-1} starting from 100% buffer a) to afford 12 mg (51%) of cyanocobalamin-*b*-ethyl-PAMA-OEt as a red solid.
MS (MeOH; ESI-pos.): m/z =1575.8 $[M+H]^+$, 788.7 $[M+H]^{2+}$, 799.3 $[M+H+Na]^{2+}$.

Page 22, lines 5-17, please rewrite as follows:

Example 11: Cyanocobalamin-*b*-propyl-PAMA-OEt

A solution of freshly prepared (*N*-3-aminopropyl-*N*-pyridin-2-ylmethyl-amino)acetic acid ethyl ester (361 ~~mol~~ µmol) in water (1 ml) is added to cyanocobalamin-*b*-acid (65.0 mg, 48.1 ~~mol~~ µmol). EDC (46.1 mg, 240 ~~mol~~ µmol) is added, and the pH is adjusted to 5.5 with NaOH 0.1 M. After stirring at RT for 15 h, HPLC analysis (sodium acetate buffer) shows about 50% of product formation. EDC (46.1 mg, 240 ~~mol~~ µmol) is added again, but prolonged stirring at room temperature does not lead to further product formation. The solvent is removed *in vacuo*, and the residue is purified by preparative HPLC (gradient a/b 0.5% min^{-1} starting from 100% acetate buffer a). The main fraction is collected, the solvent removed *in vacuo*, and the product desalted to give cyanocobalamin-*b*-propyl-PAMA-OEt in a yield of 25.8 mg (16.2 ~~mol~~ µmol, 33.3%).
ESI-MS: m/z = 806.5 $[M+1+Na]^{2+}$, 795.6 $[M+2]^{2+}$.
UV/Vis: ~~nm~~ λ/nm (~~/mol~~ ε/mol $l^{-1}cm^{-1}$) = 278.0 (8500), 361.1 (26500), 549.1 (8000).

Page 22, lines 19-29, please rewrite as follows:

Exampe 12: Cyanocobalamin-*b*-butyl-PAMA-OEt

Cyanocobalamin-*b*-acid (20.0 mg, 14.8 ~~mol~~ µmol) was dissolved in DMSO (0.8 ml). Subsequently were added DMF (2 ml) and NEt_3 (0.1 ml). In a different flask *ca.* 5 equivalents of (*N*-4-aminobutyl-*N*-pyridin-2-ylmethyl-amino)acetic acid ethyl ester (butyl-PAMA-OEt) hydrochloride (prepared via cleavage of the Boc-protected derivative by stirring in an abs. EtOH / 2 M HCl mixture (7.5 ml 4/1 v/v) overnight and subsequent removal of the volatiles *in vacuo*) was dissolved in a DMF/NEt_3 mixture (4.5 ml; 8/1 v/v). The two solutions were mixed, followed by addition of TBTU (32.1 mg, 0.1 mmol). After stirring at RT for 45 min, the solvent was removed *in vacuo*. The residue was purified by

preparative HPLC (acetate system, gradient: 1.0% min^{-1} starting from 100% buffer a) to afford 15 mg (63%) of cyanocobalamin-*b*-butyl-PAMA-OEt as a red solid.

Page 23, lines 4-13, please rewrite as follows:

Cyanocobalamin-*b*-acid (20.0 mg, 14.8 ~~mol~~ µmol) was dissolved in DMSO (0.8 ml). Subsequently were added DMF (2 ml) and NEt_3 (0.1 ml). In a different flask *ca.* 5 equivalents of [(4-amino-butyl)-pyridin-2-ylmethyl-amino]-acetic acid *9H*-fluoren-9-ylmethyl ester (butyl-PAMA-OFm) (prepared via cleavage of the Boc-protected derivative by stirring in a trifluoroacetic acid / CH_2Cl_2 mixture (4 ml 1/2 v/v) for 1 hr and subsequent removal of the volatiles *in vacuo*) was dissolved in a DMF/NEt_3 mixture (4.5 ml; 8/1 v/v). The two solutions were mixed, followed by addition of TBTU (32.1 mg, 0.1 mmol). After stirring at RT for 45 min, the solvent was removed *in vacuo*. The residue was purified by preparative HPLC (acetate system, gradient: 1.5% min^{-1} starting from 100% buffer a) to afford 15 mg of cyanocobalamin-*b*-butyl-PAMA-OFm as a red solid.

Page 23, lines 20-31, please rewrite as follows:

Example 14: Cyanocobalamin-*b*-hexyl-PAMA-OEt

Cyanocobalamin-*b*-acid (20.0 mg, 14.8 ~~mol~~ µmol) was dissolved in DMSO (0.8 ml). Subsequently were added DMF (2 ml) and NEt_3 (0.1 ml). In a different flask *ca.* 5 equivalents of (*N*-6-aminohexyl-*N*-pyridin-2-ylmethyl-amino)acetic acid ethyl ester (hexyl-PAMA-OEt) hydrochloride (prepared via cleavage of the Boc-protected derivative by stirring in an abs. EtOH / 2 M HCl mixture (7.5 ml 4/1 v/v) overnight and subsequent removal of the volatiles *in vacuo*) was dissolved in a DMF/NEt_3 mixture (4.5 ml; 8/1 v/v). The two solutions were mixed, followed by addition of TBTU (32.1 mg, 0.1 mmol). After stirring at RT for 45 min, the solvent was removed *in vacuo*. The residue was purified by preparative HPLC (acetate system, gradient: 1.0% min^{-1} starting from 100% buffer a) to afford 10 mg (41%) of cyanocobalamin-*b*-hexyl-PAMA-OEt as a red solid.
MS (MeOH, ESI-pos.): m/z = 816.9 $[M+2H]^+$, 1632 $[M+H]^+$.

Page 24, lines 4-18, please rewrite as follows:

Example 16: Cyanocobalamin-*b*-propyl-PAMA-$Re(CO)_3$

Cyanocobalamin-*b*-acid (26.7 mg, 19.8 ~~mol~~ µmol), Re([*N*-3-aminopropyl-*N*-pyridin-2-ylmethyl-amino]acetic acid)$(CO)_3$ (29.2 mg, 60 ~~mol~~ µmol), EDC (11.5 mg, 60 ~~mol~~ µmol) and HOSu (6.9 mg, 60 ~~mol~~ µmol) are dissolved in a mixture of water (5 ml) and

DMSO (0.5 ml), and the pH is adjusted to 5.5 with dilute HCl and NaOH. After 5 h of stirring at RT, HPLC analysis (acetate buffer) shows about 33% product formation. EDC and HOSu are added again. The mixture is stirred at room temperature for 3 days with addition of EDC and HOSu at 24 h intervals. The water is removed *in vacuo*, and the product is precipitated by adding diethyl ether. The oily suspension is centrifugated and decanted. Washing with diethyl ether is repeated twice until a fine precipitate forms. The crude product is dried at high vacuum, purified by preparative HPLC (gradient a/b 1% min^{-1} starting from 100% acetate buffer a), and desalted to give cyanocobalamin-*b*-propyl-PAMA-$Re(CO)_3$ in a yield of 9.1 mg (23%).

ESI-MS: m/z = 1831.7 $[M+1]^+$, 916.1 $[M+1]^{2+}$.

UV/Vis: ~~nm~~ λ/nm (~~l/mol~~ ε/mol $l^{-1}cm^{-1}$) = 278.0, 361.1, 519.9, 551.1.

Page 24, lines 20-31, please rewrite as follows:

Example 17: Cyanocobalamin-*b*-hexyl-PAMA-$Re(CO)_3$

Cyanocobalamin-*b*-acid (20.0 mg, 14.8 ~~mol~~ µmol) was dissolved in DMSO (0.8 ml). Subsequently were added DMF (2 ml) and NEt_3 (0.1 ml). In a different flask *ca.* 5 equivalents of [Re([*N*-3-aminopropyl-*N*-pyridin-2-ylmethyl-amino]acetic acid) $(CO)_3]\cdot CF_3COOH$ (prepared via Boc cleavage of the protected complex in CH_2Cl_2 and TFA·(2/1 v/v) for 1 h at 0°C, followed by removal of the volatiles at RT *in vacuo*) were dissolved in a DMF/NEt_3 mixture (4.5 ml; 8/1 v/v). The two solutions were mixed, followed by addition of TBTU (32.1 mg, 0.1 mmol). After stirring at RT for 45 min, the solvent was removed *in vacuo*. The residue was purified by preparative HPLC (acetate system, gradient: 2.0% min^{-1} starting from 100% buffer a) to afford 11 mg (40%) of cyanocobalamin-*b*-hexyl-PAMA-$Re(CO)_3$.

MS (MeOH, ESI-pos.): m/z=936.5 $[M+2H]^{2+}$, 948.3 $[M+H+Na]^{2+}$, 1873.8 $[M+H]^+$.

Page 24, line 33 to page 25, line 4, please rewrite as follows:

Example 18: Cyanocobalamin-*d*-propyl-PAMA-OEt

Cyanocobalamin-*d*-acid (9.3 mg, 6.9 ~~mol~~ µmol) was reacted with (*N*-3-aminopropyl-*N*-pyridin-2-ylmethyl-amino)acetic acid ethyl ester (7 ~~mol~~ µmol) and EDC (6.6 mg, 34 ~~mol~~ µmol) as described for the synthesis of cyanocobalamin-*b*-propyl-PAMA-OEt (Example 11). The product was isolated in a yield of 3.6 mg (33%)

ESI-MS: m/z = 1612 $[M+Na]^+$, 1590 $[M+1]^+$, 806 $[M+1+Na]^{2+}$, 795.1 $[M+2]^{2+}$.

UV/Vis: ~~nm~~ λ/nm (~~l/mol~~ ε/mol $l^{-1}cm^{-1}$) = 279.0 (13400), 361.1 (23300), 549.1 (7200).

Page 25, lines 6-14, please rewrite as follows:

Example 19: Cyanocobalamin-*d*-propyl-PAMA-Re(CO)$_3$

Cyanocobalamin-*d*-acid (20.0 mg, 14.8 ~~mol~~ µmol) was dissolved in DMSO (1.5 ml). Subsequently were added DMF (2 ml) and NEt_3 (0.1 ml). In a different flask *ca.* 5 equivalents of Re([*N*-3-aminopropyl-*N*-pyridin-2-ylmethyl-amino]acetic acid)(CO)$_3$ were dissolved in a DMF/NEt_3 mixture (4.5 ml; 8/1 v/v). The two solutions were mixed, followed by addition of TBTU (32.1 mg, 0.1 mmol). After stirring at RT for 45 min, the solvent was removed *in vacuo*. The residue was purified by preparative HPLC (acetate system, gradient: 2.0% min^{-1} starting from 100% buffer a) to afford 20 mg (73%) of cyanocobalamin-*d*-propyl-PAMA-Re(CO)$_3$.

Page 25, lines 16-24, please rewrite as follows:

Example 20: Cyanocobalamin-*b*-propyl-His-OMe

Cyanocobalamin-*b*-acid (20.0 mg, 14.8 ~~mol~~ µmol) was dissolved in DMSO (0.8 ml). Subsequently were added DMF (2 ml) and NEt_3 (1 ml). In a different flask about 4 equivalents of methyl 3-aminopropyl-*N*--Teoc-histidinate were dissolved in DMF. The mixtures were added together, and TBTU (32.1 mg; 0.1 mmol) was added. The mixture was stirred for 45 min, and subsequently evaporated to dryness *in vacuo*. Purification by preparative HPLC (acetate system; gradient: 2.0% per min, starting from buffer a) afforded 16 mg of a red solid. (67%).

MS (MeOH; ESI-pos.): m/z= 1710.4 $[M+H]^+$, 855.0 $[M+2H]^{2+}$, 866.7 $[M+Na+H]^{2+}$.

Page 26, lines 1-12, please rewrite as follows:

Example 21: Cyanocobalamin-*b*-propyl-His-Re(CO)$_3$

Cyanocobalamin-*b*-acid (20.0 mg, 14.8 ~~mol~~ µmol) was dissolved in DMSO (0.8 ml). Subsequently were added DMF (2 ml) and NEt_3 (0.1 ml). In a different flask *ca.* 5 equivalents of [Re(methyl 3-aminopropyl-*N*--Teoc-histidinate)(CO)$_3$]·CF_3COOH (prepared via Boc-cleavage of the protected complex in CH_2Cl_2 and TFA·(2/1 v/v) for 1 h at 0°C, followed by removal of the volatiles at RT *in vacuo*) were dissolved in a DMF/NEt_3 mixture (4.5 ml; 8/1 v/v). The two solutions were mixed, followed by addition of TBTU (32.1 mg, 0.1 mmol). After stirring at RT for 45 min, the solvent was removed *in vacuo*. The residue was purified by preparative HPLC (acetate system, gradient: 2.0%

min^{-1} starting from 100% buffer a) to afford 7 mg (73%) of cyanocobalamin-*b*-propyl-His-$Re(CO)_3$

MS (MeOH; ESI-pos.): 911.6 $[M+2H]^{2+}$, 923.2 $[M+H+Na]^{2+}$, 933.9 $[M+2Na]^{2+}$, 1822.1 $[M+H]^+$, 1845.6 $[M+Na]^+$.

Page 26, lines 14-27, please rewrite as follows:

Example 22: Cyanocobalamin-*b*-ethyl-Triamine

Triethylenetetramine (55.4 ~~µl~~ µl, 369 ~~µmol~~ µmol) was dissolved in a mixture of DMF (2.5 ml) and water (2.5 ml). KCN (9.6 mg, 147 ~~µmol~~ µmol) was added, and the pH was adjusted to 6 by addition of aqueous HCl. Cyanocobalamin-*b*-acid (10.0 mg, 7.4 ~~µmol~~ µmol), EDC (5.7 mg, 29 ~~µmol~~ µmol) and HOSu (3.4 mg, 29 ~~µmol~~ µmol) were added. The same amounts of EDC and HOSu were added after 6 h, 24 h, 48 h and 120 h. HPLC analysis (acetate buffer) exhibited slow product formation, reaching a 75% conversion after 48 h which was not exceeded with prolonged stirring. After stirring for 144 h, the solvent was removed *in vacuo* and the product was purified by preparative HPLC using aqueous TFA 0.1% as buffer a and methanol as solvent b, with a gradient of 1% min^{-1} starting from 80% buffer a. The product was isolated as cyanocobalamin-*b*-ethyl-Triamine x 3TFA in a yield of 7.5 mg (55%).

ESI-MS: m/z = 743.1 $[M+2]^{2+}$.

UV/Vis: ~~nm~~ λ/nm (~~l/mol~~ ε/mol $l^{-1}cm^{-1}$) = 278.0 (13000), 316.0 (23100), 519.0 (6500), 549.0 (7200).

Page 26, lines 29-36, please rewrite as follows:

Example 23: Cyanocobalamin-*b*-ethyl-Triamine-$Re(CO)_3$

Cyanocobalamin-*b*-ethyl-Triamine (5 mg, 2.7 ~~µmol~~ µmol) and $(Et_4N)_2[ReBr_3(CO)_3]$ (2.2 mg, 2.9 ~~µmol~~ µmol) were stirred in phosphate buffer, pH 7.4 (0.1 M, 0.33 ml) at 50°C. After 1 h, HPLC analysis showed full conversion of the starting materials into one product. After 4 h, the reaction mixture was desalted to give a product which is, according to HPLC analysis, a mixture of two stereoisomers in an approximate ratio of 2/1. The same pattern of two stereoisomers was found on labeling of cyanocobalamin-*b*-ethyl-Triamine with ^{99m}Tc.

ESI-MS: m/z = 1755.9 $[M+1]^+$, 878.5 $[M+2]^{2+}$.

Page 29, lines 1-18, please rewrite as follows:

Example 27: General labeling procedure

Solutions of the precursor $[^{99m}Tc(OH_2)_3(CO)_3]^+$ were prepared out of $[^{99m}TcO_4]^-$ using a boranocarbonate kit as described by Alberto et al. (J. Am. Chem. Soc. 123, 3135-3136). A 10 ml glass vial with rubber stopper was flashed with N_2. 20 ~~µl~~ µl of a solution of cyanocobalamin derivative (0.01 M in water), 20 ~~µl~~ µl of MES buffer (1.0 M) and 200 ~~µl~~ µl of a $[^{99m}Tc(OH_2)_3(CO)_3]^+$ solution were added and the reaction mixture was kept at 75°C for 1 to 2 hours. HPLC analyses with ~~ß-detection~~ γ-detection was performed to verify full conversion of the ^{99m}Tc species. Under these conditions, ester protecting groups in the chelators were cleaved to give the carboxylato complexes.

For *in vivo* studies and for binding studies to the transport vectors, very high specific activity was demanded. Therefore, 100 ~~µl~~ µl of the labeled solution were injected to an analytical HPLC system to separate the hot from the cold vitamin derivative. The eluate fraction with the highest gamma activity (ca. 300 ~~µl~~ µl) was diluted with normal saline to a concentration of 10 µCi per animal before *i.v.* injection. Separation condition were: acetate buffer, XTerra RP8 column, gradient: 0% methanol (0 min), 30% methanol (15 min), 100% methanol (25 min) for the *b*- and *d*-derivatives, and the TEAP system as described by Schibli et al. (Bioconjugate Chem. 2000, 343-351) for the other compounds.

Page 29, lines 20-30, please rewrite as follows:

Example 28: Preparation of transcobalamin II (TC II) from rabbit whole blood.

TC II is purified by affinity chromatography on a cyanocobalamin-agarose matrix (Sigma). The gel (5 ml) is first washed with 200 ml 50 mM Tris / 1 M NaCl, pH 8.0, afterwards with 200 ml 0.1 M glycine / 0.1 M glucose / 1 M NaCl pH 10, and again with 200 ml 50 mM Tris / 1 M NaCl. 200 ml of twice centrifuged whole blood (first time 5000 rpm 15 min, second time 20'000 rpm 20 min at 4°C) is applied to the affinity column, and the column washed sequentially as before. Bound TC II is eluted with 20 ml 4.0 M guanidine HCl / 50 mM Tris pH 8.0, and in a second step with 7.5 M guanidine HCl / 50 mM Tris pH 8.0. Most of the bound TC II elutes already with 4 M guanidine HCl. Probes are dialyzed extensively against H_2O for 2 days at 4°C. Typical yields are 5 – 30 nmol/l which translates into 7.5 –10 ~~ßg~~ µg of TC II (MW: 50 kDa) per rabbit.

Page 31, lines 9-21, please rewrite as follows:

Example 34: Biodistribution of radiolabeled cyanocobalamin derivatives in mice (Fig. 3, 4, 5, 6)

For biodistribution studies with ^{57}Co-cyanocobalamin, 0.2 μCi / 1 ng of the radiolabeled cyanocobalamin is mixed with 180 μl normal saline and injected *i.v.* in tumor bearing balb/c mice (syngeneic mouse melanoma B16-F10). After a specified time (5 min to 24 h), animals are sacrificed, the organs weighted and counted on a gamma counter. For biodistribution studies with ^{99m}Tc-labeled cyanocobalamin, 10 μCi / 0.5 ng of the radiolabelled cyanocobalamin is mixed with normal saline and used as before. For biodistribution with ^{111}In-labeled cyanocobalamin, 2 ~~mCi~~ μCi / 5 ng of the radiolabeled cyanocobalamin is mixed with normal saline and used as before. To study the effect of Vitamin B12 deficient food, the biodistribution of labeled cyanocobalamin is compared in mice fed with normal food with the biodistribution in mice fed with vitamin B12 deficient food for a period of 2 weeks.